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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/774,708 | 02/09/2004 | Kenneth Beaman | 112461-021 | 9549 |

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| EXAMINER | |
|---|---|
| RINAUDO, JO ANN S | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1644 | |

DATE MAILED: 11/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/774,708 | BEAMAN, KENNETH | |
| | Examiner | Art Unit | |
| | Jo Ann Rinaudo | 1644 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *05 October 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-122* is/are pending in the application.

4a) Of the above claim(s) *7-14,17-33 and 36-122* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,15,16,34 and 35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 February 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

1. Claims 1-122 are pending.

2. Applicant's election without traverse of Group I (Claims 1-6, 15, 16, 34, and 35) in a reply filed on 5 October 2005 is acknowledged.

3. Claims 7-14, 17-33, and 36-122 are withdrawn from further consideration by the Examiner, under 37 C.F.R. § 1.142(b), as being drawn to nonelected inventions.

4. An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification or in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)). The specification on page 1 should be amended to list the priority application, 60/446,499, upon which priority is claimed.

5. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention *to which the claims are directed.*

6. The use of trademarks has been noted in this application (e.g. Coulter on page 12). Each letter of the trademarks should be capitalized wherever it appears and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112.

> *The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.*

8. Claims 1-4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

9. Claims 1-4 are indefinite in the recitation of "RTF activity" because its characteristics are not known. The term is not defined in the claims and the specification does not provide a standard for ascertaining the "RTF activity". Therefore one of ordinary skill in the art would not be reasonably appraised of the metes and bounds of the invention.

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> *The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.*

11. Claims 1-6, 15, 16, 34 and 35 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of inhibiting regeneration and tolerance factor (RTF) by administering to a subject an effective amount of an anti-RTF antibody (Claim 6); wherein the administration leads to apoptosis of ovarian carcinoma cells (Claim 16), and wherein the subject is a mammal (Claim 34) and a human (Claim 35), does not reasonably provide enablement for a method of modulating inflammatory and immune responses in a subject in need thereof, the subject having a first level of regeneration and tolerance factor (RTF) activity, and the method comprising altering the first level of RTF activity to a second level of RTF activity (Claim 1); wherein the modulation of the immune response is immune activation and wherein the second level of RTF activity is lower than the first level of RTF activity (Claim 2); wherein the method of enhancing the immune response is by inhibiting RTF activity (Claim 3); wherein the method of inhibiting RTF activity is by administering to the subject an effective amount of a RTF antagonist (Claim 4); wherein the antagonist is selected from the group consisting of small molecules, peptides, antibodies, or a fragment thereof (Claim 5); wherein the antibody is selected from the group consisting of monoclonal antibodies and polyclonal antibodies (Claim 6); wherein the activation of the immune response leads to apoptosis of cancer cells (Claim 15); wherein the cancer cell is ovarian carcinoma cell (Claim 16); wherein the subject is a mammal (Claim 34); and wherein the subject is a human (Claim 35). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

12. Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, and the amount of experimentation required to enable one skilled in the art to practice the invention.

13. The specification provides no guidance for a method of "modulating inflammatory or immune responses" and "immune activation" (Claims 1, 2-6, 15, 16, 34 and 35). The specification defines modulating inflammatory and immune responses to include "both immune activation and the inhibition of the inflammatory responses" (see page 4, lines 24-26, in particular). Activation and inhibition of the inflammatory responses are mutually exclusive. In addition, an immune response is characterized by the coordinated reaction of cells, tissues and molecules (see Abbas et al. page 1, lines 1-5, in particular). Further, the immune response consists of innate and adaptive immunity (see Abbas et al., page 3, column 2, Innate and Adaptive Immunity, and Figure 1-3, in particular). Innate immunity involves specialized cells, such as Natural killer cells (NK cells) (see Abbas et al., page 4, column 1, lines 4-9, in particular). Adaptive immunity is divided into humoral and cell-mediated immunity, each consisting of different and overlapping cell types and mediator molecules (see Abbas et al., page 4, column 2, Types of Adaptive Immunity, in particular). Moreover, the inflammatory response also involves the complex reaction of the innate immune system in vascularized tissues that involves the accumulation and activation of leukocytes, release of cytokines (see Abbas, et al., page 25, column 2, paragraph 2; page 26; and page 27, Figure 2-5, in particular). Thus, the modulating of the inflammatory and immune responses involves various cell types, mediator molecules, as well as the interaction of tissues, as described supra. Therefore, in view of the lack of guidance in the specification and in view of the discussion above one of skill in the art would be required to perform undue experimentation in order to practice a method for modulating of the inflammatory and immune responses, as recited in the instant claims.

14. The specification does not provide sufficient enabling disclosure of "level of regeneration and tolerance factor (RTF) activity" and "altering the first level of RTF activity to a second level of RTF activity" (Claims 1, 2-6, 15, 16, 34 and 35). The specification discloses that RTF is the "$\alpha$ -subunit of $\alpha$2-isoforms of vacuolar ATPase (see page 5, line 31, in particular). The

specification only provides examples of an *in vitro* ATPase assay and *in vitro* induction of apoptosis using anti-RTF antibodies (see pages 10 and 11, Examples 2 and 3, in particular). The specification provides no standard in which to measure the level of RTF activity. The specification provides no definition of the first level of RTF activity or the second level of RTF activity. Therefore the skilled artisan cannot envision a method of "altering the first level of RTF activity to a second level of RTF activity". Other than the ATPase activity and induction of apoptosis, the specification does not disclose any other "regeneration and tolerance factor (RTF) activity", therefore the skilled artisan cannot envision all the other possible "regeneration and tolerance factor (RTF) activity", recited in the instant claims.

15. The specification does not provide sufficient enabling disclosure of how to make "RTF antagonist", other than an anti-RTF antibody (Claims 4 and 5). The specification defines antagonist as "acts by inhibiting cellular expression of RTF" and includes antisense nucleic acid, RNA interfereince (RNAi), and small interfering double stranded RNA (siRNA) (see page 7, lines 12-25, in particular). A person of skill in the art is not enabled to make and use ANY "RTF antagonist" encompassed by the full breadth of the claims. Therefore the skilled artisan cannot envision a method for inhibiting RTF activity by administering a RTF antagonist, other than an anti-RTF antibody.

16. The specification does not provide sufficient enabling disclosure for a method of immune activation wherein the "activation of the immune response leads to apoptosis of cancer cells" (Claim 15). Boomer et al. teaches that anti-RTF antibody does not induce apoptosis in unstimulated Jurkat human leukemic T cell line (see page 962, column 1, Anti-RTF antibody induces apoptosis; and page 966, Figure 4, in particular). The method is unpredictable because not all cancer cells undergo apoptosis. Therefore, one of skill in the art would be required to perform undue experimentation in order to practice a method for "activation of the immune response leads to apoptosis of cancer cells, other than ovarian carcinoma cells, as recited in the instant claims.

17. Reasonable correlation must exist between the claims and the enablement set forth. In view of the quantity of experimentation necessary, the limited working examples, the nature of

the invention, the state of prior art, the unpredictability of the art and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

18. Claims 1-6, 15, 16, 34 and 35 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

19. Applicant is in possession of a method of inhibiting regeneration and tolerance factor (RTF) by administering to a subject an effective amount of an anti-RTF antibody (Claim 6), wherein the administration leads to apoptosis of ovarian carcinoma cells (Claim 16), and wherein the subject is a mammal (Claim 34) and a human (Claim 35). Applicant is not in possession of a method of modulating inflammatory and immune responses in a subject in need thereof, the subject having a first level of regeneration and tolerance factor (RTF) activity, and the method comprising altering the first level of RTF activity to a second level of RTF activity (Claim 1); wherein the modulation of the immune response is immune activation and wherein the second level of RTF activity is lower than the first level of RTF activity (Claim 2); wherein the method of enhancing the immune response is by inhibiting RTF activity (Claim 3); wherein the method of inhibiting RTF activity is by administering to the subject an effective amount of a RTF antagonist (Claim 4); wherein the antagonist is selected from the group consisting of small molecules, peptides, antibodies, or a fragment thereof (Claim 5); wherein the antibody is selected from the group consisting of monoclonal antibodies and polyclonal antibodies (Claim 6); wherein the activation of the immune response leads to apoptosis of cancer cells (Claim 15); wherein the cancer cell is ovarian carcinoma cell (Claim 16); wherein the subject is a mammal (Claim 34); and wherein the subject is a human (Claim 35).

20. There is insufficient written description in the specification for a method of "modulating inflammatory and immune responses" in a subject in need thereof, the subject having a first "level of regeneration and tolerance factor (RTF) activity", and the method comprising "altering the first level of RTF activity to a second level of RTF activity" (Claims 1, 2-6, 15, 16, 34 and 35). The specification does not disclose what immune response (innate or adaptive and within adaptive, humoral or cellular) will be modulated. In addition, there is insufficient possession of

"level of regeneration and tolerance factor (RTF) activity" and "altering the first level of RTF activity to a second level of RTF activity" that would be necessary to establish the relevant functional characteristics. Therefore, the skilled artisan cannot envision a method of "modulating inflammatory and immune responses" in a subject in need thereof, the subject having a first "level of regeneration and tolerance factor (RTF) activity", and the method comprising "altering the first level of RTF activity to a second level of RTF activity".

21. There is insufficient written description of "RTF antagonist" (Claims 4 and 5). The specification does not disclose the structural and functional properties associated with "RTF antagonist". Therefore, the skilled artisan cannot envision all the contemplated "RTF antagonist", other than an anti-RTF antibody used in a method of modulating inflammatory and immune responses in a subject in need thereof, the subject having a first level of regeneration and tolerance factor (RTF) activity, and the method comprising altering the first level of RTF activity to a second level of RTF activity. There is insufficient written description of a method of immune activation wherein the "activation of the immune response leads to apoptosis of cancer cells.

22. Consequently, conception cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC1993). The Guidelines for the Examination of Patent Application Under the 35 U.S.C.112, ¶ 1"Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 20001, see especially page 1106 3rd column).

23. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

24. Applicant is directed to the final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

25. No claim is allowed.

26. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jo Ann Rinaudo whose telephone number is 571.272.8143. The examiner can normally be reached on M-F, 8:30AM - 5PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571.272.0841. The fax phone number for the organization where this application or proceeding is assigned is 571.273.8300.

27. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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11/17/2005

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